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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,302	09/22/2005	Michihiro Ohnishi	09947.0002-00000	1171

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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,302	OHNISHI ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,8-13 and 16-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,8-13 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12 November 2010 has been entered.

Status of the Claims

2. This action is in response to papers filed 12 November 2010 in which the previous rejections were traversed. Applicant's arguments have been thoroughly reviewed and are discussed below.

The previous rejections in the Office Action dated 14 May 2010 under 35 U.S.C. 103(a) are re-stated along with further supporting evidence of obviousness. The previous rejection under 35 U.S.C. 112, first paragraph is maintained.

Claims 1, 3-4, 8-13 and 16-18 are under prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Claim 18 defines the gap part as having “a fixed sectional size”. Applicant points to ¶ 31-33, 44 and 46 for support of the newly added claims. The cited passages and the entire specification have been reviewed for support of the newly defined gap, however no support has been found. Therefore, the new claim appears to introduce subject matter that was not described in the originally filed specification.

Response to Arguments

5. In the response of 13 September 2010, Applicant asserts that paragraph 29 and Figure 4 provide support for the "fixed sectional size” because the passage and figure clearly define a protruding part as a component of the substrate itself thereby defining a fixed sectional size.

The citation is noted. However, Claim 1 defines protruding parts in both the first and second substrate and a moveable protruding part for either the first or second substrate. Paragraph 29 appears to define a protruding part in only one of the substrates, not both as required by Claim 1. Therefore, the limitations of Claim 18 appear to define an embodiment not described in the specification.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 3-4, 7 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zenhausern et al (U.S. Patent Application Publication No. 2004/0011650, filed 22 July 2002 and Quake et al (WO 02/40874, published 23 May 2002) Wilding (U.S. Patent No. 5,587,128, issued 24 December 1996) and/or in view of Murphy (U.S. Patent No. 6,743,516, issued 1 June 2004) and/or Reinhardt et al (U.S. Patent No. 4,015,031, issued 29 March 1977).

Regarding Claim 1, Zenhausern teaches a microchip having a microchannel formed in a substrate using known techniques (¶ 48), wherein the microchannel is provided with a gap wherein adjacent sides of the channel (grooved parts) have protruding parts (constrictions) forming the gap wherein the first or second protruding part is movable (i.e. "movable array of constrictions within the channel" ¶ 61 and Fig. 2).

Zenhausern specifically teaches that the channeled structure "may be fabricated in a variety of ways" (¶ 48) but does not specifically teach a channel formed between two grooved substrates. Zenhausern further teaches the channels are constricted but does not teach a size of the particle relative to the constriction (¶ 47, 252).

However, channel formation between opposing grooved substrates having protrusions movable to block beads of a predetermined size was well known in the art at

the time the invention was made as taught by Quake (¶ 21 and 208). Quake further teaches that the protruding valves facilitate retention and analysis of analytes on the particles (¶ 314).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the grooved substrates forming protruding valves of Quake to the device of Zenhausern. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the suggestion of Zenhausern to use any of a variety of known techniques to construct the channels. One of ordinary skill would have been further motivated to do so for the benefit of facilitating retention and analysis of analytes on the particles as taught by Quake (¶ 314).

Zenhausern teaches the surface of the channel is treated to prevent components of the reaction mixture from sticking to the surface (¶ 49) and teaches the generic organosilane surface treatment e.g. dimethylchlorosilane (¶ 196). Quake, in a similar fashion teaches a generic silane surface treatment agent (¶ 235) but the references do not teach a triethylchlorosilane (TECS).

However, alkyl chlorosilane surface coatings were well known in the art at the time the invention was made as taught by Wilding, Murphy and Reinhardt.

Wilding teaches coating microfluidic channels using alkyl chlorosilane (e.g. TMCS) for blocking biomolecule interaction with the substrate (Column 15, lines 30-40).

Furthermore, chlorosilane surface treatments including triethylchlorosilane (TECS)) were well known in the art at the time the invention was made as taught by Reinhardt, Murphy.

Murphy teaches that TMCS and TECS provide highly durable hydrophobic coatings (Abstract, Fig. 4) and specifically teaches that a capping layer of alkyl chlorosilane adds to the durablilty of the coating (Column 2, lines 1-15). Murphy also provides an example wherein one part TECS is used in the coating mixture to provide a contact angle of greater than 65 degrees (Example XXIV).

Reinhardt also teaches chlorosilanes useful for providing a hydrophobic surface on silica include TECS (Column 4, lines 53-56). All of this suggests that TECS provides a desirable hydrophobic surface that would function to provide hydrophobicity to the surface.

The claimed TECS differs from the structure of TMCS by adding a carbon to teach of the alkyl groups of the chlorosilane. Adding carbons to alkyl groups is known to increase hydrophobic properties of a compound. Therefore, the artisan wishing to provide a surface that was non-sticking to aqueous reagents (such as Zenhausern and Quake) would have been motivated to maximize hydrophobic properties of the surface. To do so, the artisan would reasonably add a carbon to the TMCS of Wilding to obtain the TECS as claimed. To do so would increase hydrophobicity of the surface to thereby maximize non-sticking as desired.

In addition, the courts have stated:

> similar properties may normally be presumed when compounds are very close in structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also In re

> Grabiak, 769 F.2d 729,731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972) (see MPEP 2144.08(d)).

The courts have also stated:

> [c]ompounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977). See also In re May, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (stereoisomers prima facie obvious) (see MPEP 2144.09).

For all the above reasons, the substitution of a triethylchlorosilane for the alkyl chlorosilanes of Zenhausern or Quake or the trimethylychlorosilane of Wilding would be considered an obvious variation over the prior art.

Regarding Claim 3, Zenhausern et al disclose the microchip wherein the gap is formed by opposed protruding parts (Fig. 2, ¶ 252).

Regarding Claim 4, Zenhausern et al disclose the microchip wherein the channel has protruding parts within the channels (Fig. 1 and 2) wherein the constriction inserts the protruding parts of the channels into the grooved channel of the opposing substrate, which are formed by bonding upper and lower substrate (¶ 48 and ¶ 60). Hence, the protrusion formed in one substrate is within the channel structure of the other substrate.

Regarding Claim 7, Zenhausern et al disclose the microchip wherein the inner surface of the microchannel is treated with biocompatible materials to prevent non-specific binding (¶ 49-50).

Regarding Claim 16 and 17, Zenhausern teaches the device wherein the substrate is glass or quartz (¶ 44) and Quake teaches the device wherein the substrates are made of glass or quartz (¶ 129 & 240).

Regarding Claim 18, Quake teaches the gap part (i.e. protrusion) is an "appropriate size and shape and spaced relative to one another" (¶ 208). The claim defines a "fixed sectional size".

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111). The claims are given the broadest reasonable interpretation consistent with the broad claim language and specification wherein neither sectional size nor fixed sectional size is defined. Given the broadest reasonable interpretation, the projections of Quake are encompassed by the claim because the projections have a defined size and spacing.

8. Claims 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zenhausern et al (U.S. Patent Application Publication No. 2004/0011650, filed 22 July

2002) and Quake et al (WO 02/40874, published 23 May 2002) in view of Wilding (U.S. Patent No. 5,587,128, issued 24 December 1996) and/or Murphy (U.S. Patent No. 6,743,516, issued 1 June 2004) and/or Reinhardt et al (U.S. Patent No. 4,015,031, issued 29 March 1977) as applied to Claim 1 above and further in view of Lough et al (U.S. Patent No. 5,900,481, issued 4 May 1999) or Smith et al (U.S. Patent No. 6,270,970, issued 7 August 2001).

Regarding Claims 8-13, Zenhausern et al disclose a microchip having a microchannel formed in a substrate using known techniques (¶ 48), wherein the microchannel is provided with a gap having a sectional size variable by a movable protruding part i.e. movable array of constrictions (¶ 61, 252).

Zenhausern et al further teach the channels are constricted to capture nucleic acid-immobilized on beads for analysis wherein the channel diameter is less than 10μm (¶ 47, 252) but they do not specifically teach the bead diameter or hydroxyl functional groups for nucleic acid attachment. However, silica particles of less than 10μm having hydroxyl functional groups were well known and routinely practiced in the art at the time the claimed invention was made as taught by Lough et al.

Lough et al teach silica microbeads having a preferred size of less than 10μm (Column 3, lines 13-15, 25-26) and hydroxyl functional groups (Fig.2) wherein the surface is treated with a silane coupling agent (Fig. 2, Columns 3-4) whereby the nucleic acids for detecting are absorbed onto the surface of the beads (Abstract). Lough et al further teach the functionalization of the beads and surfaces provides differential immobilization chemistry between the bead-surface-nucleic acids (Abstract).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the bead and surface functionality of Lough et al to the particles of Zenhausern. One of ordinary skill in the art would have been motivated to do so based on the preferred differential immobilization of Lough (Abstract).

Smith also teach silica microbeads having a preferred size of less than 10μm (Column 12, lines 16-32) and immobilization-specific functional groups (Column 14, lines 45-56) wherein the surface is treated with a silane coupling agent (Column 14, line 57-Column 15, line12) whereby the nucleic acids for detecting are selectively absorbed onto and released from the surface of the beads based on the presence and/or concentration of chaotropic salts (Column 16, line 58-Column 17, line 25) whereby the salts provide the nucleic acids in an unfolded stated (Column 10, lines 43-57).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the chaotropic salts of Smith et al to the hybridization methods of Zenhausern and Lough. One of ordinary skill in the art would have been motivated to do so for the expected benefit of providing unfolded nucleic acids that are more thermodynamically stable than folded nucleic acids to thereby favor hybrid formation (Smith et al, Column 10, lines 43-57).

Response to Arguments

Applicant argues that the Office has failed to identify any reason why one of ordinary skill would have chosen TECS as claimed. Applicant further argues that

Murphy fails to establish the functional equivalence of TMCS and TECS as surface treatments and therefore there is no reason to replace TMCS with TECS. Applicant acknowledges that Murphy discloses a combination of TMCS and TECS to create a hydrophobic surface but argues that Murphy never treats a surface with TECS and further argues that Murphy does not teach TMCS and TECS are functional equivalents and therefore does not provide a reason to replace TMCS with TECS.

The arguments have been considered but are not found persuasive. As Applicant notes, Murphy does teach an embodiment using a mixture of TMCS and TECS (Example XXIV) thereby providing a surface decorated with TECS as claimed. Furthermore, newly cited reference Reinhardt teaches that organosilanes suitable for providing hydrophobic surface treatments include TMCS and TECS (Column 4, lines 53-60). Thus it is an art-recognized fact that TMCS and TECS are suitable for providing hydrophobic surface.

Absent evidence to the contrary, it would have been obvious to replace TMCS with TECS based on the functional similarity. Furthermore, the claimed TECS differs from the TMCS by additional CH_2 groups. The courts have clearly stated that the compounds differing by addition of CH_2 groups are sufficiently close that one would expect them to possess similar properties.

> homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977). See also In re May, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (stereoisomers prima facie obvious) (see MPEP 2144.09).

Absent evidence to the contrary, it is maintained that it would have been obvious to replace TMCS with TECS because one would have expected them to possess similar properties.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BJ Forman

Primary Examiner
Art Unit 1634

/BJ Forman/
Primary Examiner, Art Unit 1634